

REMARKS

Claims 1-66 are pending. Claims 31-38, 43-46, 49, 50, 54-58, and 61 are under examination. Claims 31 and 46 have been amended. Support for the amendments can be found throughout the specification and the claims as filed. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Rejection Under 35 U.S.C. § 101

The rejection of claims 31-38, 43-46, 49, 50, 54-58 and 61 under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter is respectfully traversed. Applicant respectfully submits that the claimed methods are directed to statutory subject matter.

Applicant respectfully submits that a *prima facie* case that the claims are directed to non-statutory subject matter has not been established. As set forth in MPEP § 2106, 35 U.S.C. § 101 defines four categories of inventions as patentable subject matter, namely processes (methods), machines, manufactures and compositions of matter. The claims are directed to a method for determining a nuclear packing efficiency (NPE) for a cell or population of cells, and includes the steps of “measuring a biochemical component (BC) of the nucleus of a cell” and “measuring a spatial displacement of the nucleus (SDN) of the cell.” Applicant respectfully submits that the Office Action sets forth no rationale that the claims are not directed to statutory method claims. At best, the Office Action alleges that the claims “contain a non-statutory embodiment wherein the method of determining a nuclear packing efficiency as claimed can be carried out on a computer involving the manipulation of data without a concrete, tangible and useful result.” However, Applicant respectfully submits that merely because a method can include the use of a computer to analyze data in no way changes the fact that the claim is directed to a method and is therefore statutory. As set forth in MPEP 2106 (IV)(C), “[T]he subject matter courts have found to be outside of, or exceptions to, the four statutory categories of invention is limited to abstract ideas, laws of nature and natural phenomenon.” Applicant respectfully submits that the Office Action sets forth no rationale that the claims are directed to the so-called “judicial exceptions” of an abstract idea, law of nature or natural phenomenon. The fact that some aspects of the claimed method “can be carried out on a computer” does not change the claim from a statutory method to a non-statutory “abstract idea, law of nature or natural phenomenon.”

The Office Action asserts in the sentence bridging pages 2-3 that the steps of “measuring of biochemical component (BC) and spatial displacement of the nucleus recited in steps (a)(1) and (a)(2) can be done from data residing in the memory of a computer and not directly from a physical sample. Applicant respectfully requests clarification of how a “measuring” step can be performed without a physical sample. It is respectfully submitted that such an interpretation is contrary to the meaning of “measuring.” Furthermore, claim 31 recites in step (a)(1) “measuring a biochemical component (BC) of the nucleus of a cell” and in step (a)(2) “measuring a spatial displacement of the nucleus (SDN) of the cell.” It is unclear how such a measurement can be made without a cell. The fact that a measurement of a biochemical component or the spatial displacement of the nucleus of a cell can be made and potentially stored on a computer does not change the fact that the measurement was made and certainly does not convert a statutory method claim to a non-statutory “abstract idea, law of nature or natural phenomenon.”

Applicant further respectfully disagrees with the assertion in the Office Action on page 3 that “the claims currently have a non-statutory embodiment which does not meet the standard of being concrete, tangible and useful.” First, it is unclear what “a non-statutory embodiment” is, because if the claim is considered to have “an” embodiment that is non-statutory but other embodiments that are statutory, then the Office Action is acknowledging the statutory nature of the claims. Second, MPEP § 2106 (IV)(C)(2), states:

A claimed invention is directed to a practical application of a 35 U.S.C. 101 judicial exception when it:

- (A) “transforms” an article or physical object to a different state or thing; or
- (b) otherwise produces a useful, concrete and tangible result, based on the factors discussed below. [emphasis added]

Thus, the transformation of an article or physical object or the production of a useful, concrete and tangible result, as acknowledged in the Office Action on page 3, is assessed as to the patentability of a judicial exception of an abstract idea, law of nature or natural phenomenon. However, as discussed above, Applicant respectfully submits that the claims are directed to statutory subject matter, not to a judicial exception. Moreover, the Office action states in the sentence bridging pages 3-4 that a “process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate

subject matter and is not deemed to be concrete, tangible, and useful and is therefore non-statutory." As discussed above, the measuring steps specifically recited in the claimed methods are clearly not "solely mathematical operations."

Applicant respectfully submits that the claimed methods are directed to statutory subject matter. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 31-34, 37, 38, 43-46, 49, 50, 54-58 and 61 under 35 U.S.C. § 112, second paragraph as allegedly indefinite is respectfully traversed. Applicants respectfully submit that the claims are clear and definite.

Regarding claim 31, this claim has been amended to recite the meaning of "NPE" at its first recitation in the preamble, as requested by the Examiner. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Regarding claim 46, this claim has been amended to recite that the geometric parameter "increases along the major axis." Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102

The rejection of claims 31-38, 43-46, 49, 50 and 54-58 under 35 U.S.C. § 102(b) as allegedly anticipated by Irinopoulou et al., Anal. Quant. Cytol. Histol. 20:351-357 (1998), is respectfully traversed. Applicants respectfully submit that the claims are novel over Irinopoulou et al.

Applicant submits that Irinopoulou et al., at best, only describe indirect estimates of the spatial displacement of the nucleus (SDN). Instead of measuring nuclear volume, Irinopoulou et al. uses a surrogate for measuring DNA volume, namely DNA staining. Irinopoulou et al. discloses that tissue slices were fixed and "stained for DNA by chromomycin A3 (CA3)" (page 352, left column, second paragraph under "Sample Preparation"). Further, "3-D fluorescent images were obtained" using a confocal laser scanning microscope (page 352, second paragraph under "Image Acquisition and Analysis"). Such a measurement reflects the volume of the DNA

but not the volume of the nucleus, despite the assertion in the references that it is a measurement of nuclear volume. The specification teaches, for example, on page 2, lines 15-25, that the previous use of stained DNA as an estimate for nuclear volume fails to account for the granularity of DNA within the nucleus and the contribution of other components to nuclear volume. In contrast, the claims recite measuring a spatial displacement of the nucleus (SDN) of the cell, that is, the volume of space that is occupied by the nucleus (see specification, page 7 lines 16-20).

Applicant respectfully disagrees with the assertion in the Office Action on page 6 that each of the regression lines “have a different slope and pass through the origin of the axes,” referring to page 355, Figure 3, of Irinopoulou et al. In fact, none of the slopes shown in the graph of Figure 3 intersect at the origin, as would be expected with a reliable correlation. Thus, this reference, at best, describes indirect estimates of nuclear volume based on the flawed assumption that DNA content correlates well with nuclear volume but provides no teaching of the claimed methods that recite measuring spatial displacement of the nucleus (SDN) of the cell.

Applicant respectfully submits that the claimed methods are novel over Irinopoulou et al. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

The rejection of claims 31-34, 37, 38, 43-46, 49, 50, 54-58 and 61 under 35 U.S.C. § 103 as allegedly obvious over Irinopoulou et al., *supra*, and further in view of Baldetorp et al., Cytometry 13:577-585 (1992), is respectfully traversed. Applicants respectfully submit that the claimed methods are unobvious over Irinopoulou et al., alone or in combination with Baldetorp et al.

As discussed above, Irinopoulou et al., at best, describes the indirect measurement of nuclear volume by using a surrogate for nuclear volume, the staining of DNA. Such a measurement reflects the volume of the DNA but not the volume of the nucleus, despite the assertion in Irinopoulou et al. that it is a measurement of nuclear volume. To the contrary, Irinopoulou et al. provides no teaching or suggestion of the claimed methods for determining nuclear packing efficiency (NPE) of a cell or population of cells that recite measuring a spatial

displacement of the nucleus (SDN) of the cell. Moreover, Baldetorp et al. does not cure the deficiencies of Irinopoulou et al. Baldetorp et al., at best, describes measurement of DNA ploidy using image cytometry of human breast cancer but provides no teaching or suggestion of the claimed methods, which measure spatial displacement of the nucleus (SDN). Absent such a teaching or suggestion, Irinopoulou et al., alone or in combination with Baldetorp et al., cannot render the claimed methods obvious.

Applicant respectfully submits that the claimed methods are unobvious over Irinopoulou et al., alone or in combination with Baldetorp et al. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

Double Patenting

The rejection of claims 31-34 for obviousness-type double patenting over claims 6 and 21-23 of U.S. Patent No. 6,587,792, is respectfully traversed. Applicant respectfully requests that this rejection be held in abeyance until there is an indication of allowable subject matter.

In light of the amendments and remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

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To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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